PATENT COOPERATION TREATY

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From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

ANDERSON, J., Wayne
National Research Council of Canada
Intellectual Property Services
Building M-58, Room EG12
Ottawa, Ontario K1A 0R6
CANADA

WRITTEN OPINION

(PCT Rule 66)

Date of mailing (day/month/year)	13.08.2001
Applicant's or agent's file reference: 11041-98	REPLY DUE: within 1 month(s) and 15 days from the above date of mailing

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/CA00/00777	28/06/2000	28/06/1999

International Patent Classification (IPC) or both national classification and IPC
C12N9/00

Applicant
NATIONAL RESEARCH COUNCIL OF CANADA et al.

1. This written opinion is the first drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☒	Certain document cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 28/10/2001.

Name and mailing address of the international preliminary examining authority:
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Authorized officer / Examiner
Barnas, C

Formalities officer (incl. extension of time limits)
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I. Basis of the opinion

1. With regard to the elements of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

Description, pages:

1-45 as originally filed

Claims, No.:

1-70 as originally filed

Drawings, sheets:

1-5 as originally filed

Sequence listing part of the description, pages:

1-13, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequ nce listing has b en furnished.

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4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 3, 7-12, 17, 21-26, 31, 35-40, 44, 48, 61, 69 (all completely); 1, 13-15, 27-29, 41, 42, 45, 46, 49-59, 62-67, 70 (all partially),

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 3, 7-12, 17, 21-26, 31, 35-40, 44, 48, 61, 69 (all completely); 1, 13-15, 27-29, 41, 42, 45, 46, 49-59, 62-67, 70 (all partially).

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability;

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citati ns and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1, 2, 4-6, 13-16, 18-20, 28-30, 32-34, 41-43, 45-47, 49-60, 63, 66-68, 70 (NO)
Inventive step (IS)	Claims	27, 49-52, 54-58, 64, 65 (NO)
Industrial applicability (IA)	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

WRITTEN OPINION
SEPARATE SHEET

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Re Item I
Basis of the opinion

The examination has been restricted to the Helicobacter galactosyltransferase (see ISR).

It was not possible for the IPEA to check whether the subsequently-filed sequence listing (received 27.7.2000) constitutes added matter. Examination has therefore been carried out on the basis of the sequences or sequence listing as filed.

Re Item V
Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1: TOMB J -F ET AL: 'THE COMPLETE GENOME SEQUENCE OF THE GASTRIC PATHOGEN HELICOBACTER PYLORI' NATURE,GB,MACMILLAN JOURNALS LTD. LONDON, vol. 388, no. 6642, 7 August 1997 (1997-08-07), pages 539-547,TABEL, XP002082108 ISSN: 0028-0836 cited in the application -& DATABASE EMBL [Online] Accession AE000594, 25 August 1997 (1997-08-25) TOMB J -F ET AL: 'Helicobacter pylori 26695 section 72 of 134 of the complete genome.' XP002155834

(formerly D6) D2: WO 96 40893 A (ASTRA AB ;BERGLINDH O THOMAS (SE); MELLGAERD BJOERN L (SE); SMITH) 19 December 1996 (1996-12-19)

D3: WANG G ET AL: 'MOLECULAR GENETIC BASIS FOR THE VARIABLE EXPRESSION OF LEWIS Y ANTIGEN IN HELICOBACTER PYLORI: ANALYSIS OF THE ALPHA(1,2) FUCOSYLTRANSFERASE GENE' MOLECULAR MICROBIOLOGY,GB,BLACKWELL SCIENTIFIC, OXFORD, vol. 31, no. 4, February 1999 (1999-02), pages 1265-1274, XP000868904 ISSN: 0950-382X

(formerly D5) D4: CHAN N W ET AL: 'THE BIOSYNTHESIS OF LEWIS X IN HELICOBACTER PYLORI' GLYCOBIOLOGY,GB,IRL PRESS,, vol. 5, no. 7, 1995, pages 683-688, XP002920175 ISSN: 0959-6658 cited in the application

1. Art. 33(2) PCT, Novelty

1.1. D1 ISR discloses an isolated recombinant polynucleotide containing the coding region (nucleotides 1551-2372) for the Helicobacter pylori β-1,4-galactosyltransferase (HP0826 see Table 2, "Cell Envelope Genes", right column). Said coding region shows 100% identity to SEQ ID NO: 1. Because this polynucleotide compris s nucleotides locat d 5' to the coding region it is expected to contain of the 1,4-galactosyltransferase promoter. D1

is, therefore nov lty destroying for **claims 1, 2, 4-6, 13, 14, 29, 30, 32-34, 41-43 and 45.**

1.2. D2 discloses an isolated H. pylori polypeptide with the amino acid sequence SEQ ID NO. 1887. Said polypeptide shows 94.8% identity in a 273 amino acid overlap to the amino acid sequence SEQ ID NOs: 2 of the H. pylori β-1,4-galactosyltransferase of th specification. Because of the high sequence homology, said isolated polypeptide of D2 is regarded as β-1,4-galactosyltransferase. D2 (p. 33, ln. 8-11 and ln. 25-30) further discloses host cells which comprise a vector with an expression cassette containing the nucleic acid encoding said polypeptide. D2 also describes a method to produce said polypeptide using said host cell. D2 is therefore, novelty destroying for **claims 15, 16, 18-20, 28, 46, 47, and 53.**

1.3. D3 (p. 1268, right column) discloses a mutant H.pylori strain having deactivated the α(1,2) fucosyltransferase gene. **Claims 59, 60 and 66** are, therefore, not new.

1.4. Claims 63 embraces vaccines comprising any antigen including any immunogenic protein from the mutant H. pylori strain of claim 59. Such immunogenic proteins derived from the mutant strain, however, cannot, be distinguished from a wild type strain. Thus claim 63 embraces vaccines which cannot be distinguished from known vaccines (see eg. D2) and is, therefore, not new.

1.5. D4 (p. 686, right column, second paragraph "Activity screening") discloses a reaction mixture suitable for an enzymatic synthesis of a Helicobacter lipopolysaccharide and of a mimic of a Helicobacter lipopolysaccharide. Said disclosure is novelty destroying for **claims 67, 68 and 70.**

1.6. Claims 1, 15, 27, 29, 42, 46 and 49-58 describe "a portion" or "fragments" of a nucleic acid or a polypeptide. Said wording embraces any fragment including fragments consisting of only one nucleotide or one amino acid. Said claims and claims dependent thereon ar , therefore, also because of this reason not new.

2. Art. 33(3) PCT, Inventive Step

2.1. The isolation of a polypeptide which is encoded by a known nuclei acid repres nts a routine method which th skilled person would apply and does not comprise an inv ntive

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step. The β-1,4-galactosyltransferase with the amin acid sequence SEQ ID NO: 2 (claim 27) encoded by the known SEQ ID NO: 1 is, therefore, not inventive.

2.2. D3 (p. 686, left column, last paragraph, ln. 5-11) describes β-1,4-galactosyltransferase activities in H. pylori. Said document states that there are diff rent strains of H. pylori which differ at the genome level. D3 teaches further the isolation of homogenous enzymes and sequencing and cloning of the galactosyltransferases. The isolation of the β-1,4-galactosyltransferases with the amino acid sequences SEQ ID NOs: 2 and 10 and their coding nucleic acids SEQ ID NOs: 1 and 9 follows, therefore, the teaching of D3 and is not inventive. **Claim 27** is, therefore, not inventive.

2.3. Claims 64 and 65 are directed to vaccines containing a mutant lipopolysaccharide. The specification, however, does not shown any specific effect resulting from such vaccines. Thus, said vaccines are regarded as arbitrary modifications of known vaccines comprising wild-type lipopolysaccharides (see e.g. D2) and **claims 64 and 65** are, therefore, not inventive.

2.4. **Claims 49-52 and 54-58** relate to subject matter which the skilled person w uld provide, according to the circumstances, by applying standard methods without the use of inventive skill. Said claims are, therefore, not inventive.

Re Item VI

Certain documents cited, Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
Form D 2 WO99/40205	12.8.99	27.1.99	4.2.98

The above listed document was published after but filed before the priority date of the present application. It does, therefore, not belong to the state of the art according to Rule 64(1)(b) PCT. It will, however, become of relevance for the novelty of the claimed subject matter during regional phase examination, and if it later turns out that the priority of the present application has not been correctly claimed, also for the inventive step involved with the claimed subject matter.

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***The applicant is requested** to file new claims and/or explanations which take account of the above comments. The attention of the applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed, **Art. 34 (2) PCT**. Therefore, the applicant is asked to indicate the basis of any amendments to the claims in the application documents originally filed.*

Add it into the Cover